UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/463,276	05/12/2000	Neal L. First	96429/9085	6126

7590 12/02/2003

Teresa J Welch
Michael Best & Friedrich
One South Pinckney Street Suite 700
PO Box 1806
Madison, WI 53701-1806

EXAMINER	
WOITACH, JOSEPH T	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 12/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	pplicant(s)	
	09/463,276	FIRST ET AL.	
	Examin r	Art Unit	
	Joseph T. Woitach	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the c rresp ndence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 January 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Pri rity under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on January 8, 2003, paper number 21, has been entered.

DETAILED ACTION

This application filed May 12, 2000, is a 371 national stage filing of PCT/US98/15387, filed July 24, 1998.

Applicants' amendment filed January 8, 2003, paper number 22, has been received and entered. February 14, 2002, paper number 10, has been received and entered. Claim 15 has been canceled. Claims 1, 5 and 13 have been amended. Claims 1-14 are pending and currently under examination.

Response to Amendment

The declaration of Dr. First filed under 37 CFR 1.132 filed January 8, 2003, has been fully considered, and will be discussed to the extent it applies to the rejections set forth below.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

As noted in the advisory action mailed September 23, 2002, paper number 15, claim 1 rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is withdrawn.

The amendment to the claim has obviated the basis of the rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 12 rejected under 35 U.S.C. 102(b) as anticipated by Barnes *et al.* (Molecular Reproduction and Development, 1992 IDS reference) as evidenced by Telford *et al.* (Mol. Reprod. Dev. 26:90-100, 1990) is withdrawn.

Amendments to the method of claim 1 to encompass the use of a non-bovine nuclear material would result in a non-bovine species of NT unit, therefore the bovine embryo of Barnes *et al.* does not anticipate the instantly claimed embryo.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 12 and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Gurdon (J. Cell. Sci., 1986 IDS reference).

Applicants summarize the teaching of Gurdon and note that the recipient oocyte in Gurdon was from an amphibian and does not teach the specific use of a bovine oocyte. Applicants note the amendments to the claims to recite a mammalian recipient oocyte have been made to further clarify the invention and that they overcome the rejection. Further, Applicants note that the claims have been amended to indicate that the resulting embryo is cultured to

undergo maternal to embryonic transition. See Applicants' amendment, pages 3-6. Applicants' arguments have been fully considered and found persuasive in part.

Examiner would agree that Gurdon does not reduce to practice the methods instantly claimed, thus the specific embryos instantly claimed and that the embryos specifically disclosed in figure 6 encompass only the use of amphibian oocyte, not a bovine oocyte. However, as noted in the basis of the rejection previously set forth under 35 USC 102(b), Gurdon discuss the nuclear transfer in groups other than amphibian. In particular, Gurdon summarizes the early success of nuclear transfer in mammals (page 312, citing the work of Hoppe, Illmensee, Kelly and McGrath). Further, in the description of nuclear transfer between species, the experiments proposed focus on the analysis of affects on development of maternal factors and chromosomal factors (pages 301-302) indicating that the cultured NT unit is generated and cultured for analysis of the embryonic to maternal transition. Examiner would concede that Gurdon does not specifically make the embryos which meet the limitation of a mammalian oocyte and bovine oocyte recited in the method claims which result in the embryo of the instant claims, however, clearly Gurdon and contemplate and teach the general use of trans-species nuclear transfer for the study of development. Further, Gurdon specifically discusses the state of the art for mammalian nuclear transfer and provides an example wherein the nuclear material was from a mammal. Because a bovine is a mammal, and transpecies nuclear transfer would encompass the use of a bovine oocyte and nuclear material from a cell other than a bovine, the teachings of Gurdon anticipate, or make obvious the instantly claimed embryos. In view of the teachings of the

reference as whole, clearly the generation of other trans-species combinations, *i.e.* nuclear material of one species into a mammalian oocyte, for the study of development would be encompassed by the teachings of Gurdon.

Claims 12 and 14 stand rejected under 35 U.S.C. 102(e) as being anticipated by Stice *et al.* (WO 95/17500).

Applicants to do not specifically address the basis of the rejection in the amendment, however the declaration of Dr. First notes that Stice et al does not teach the use of differentiated cells as required by certain claims. See paragraph 7 of the declaration.

It is noted that method claims 1 and 13, which are used to generate the product of claim 12 and 14, have been amended to recite new limitations to distinguish that a bovine oocyte is used and that the nuclear material is from a different species, and that the resulting NT unit is cultured to undergo maternal to embryonic transition. However, Stice *et al.* teach nuclear transfer procedures for producing non-human chimeric animals. Specifically, nuclear transfer techniques are used to introduce the nuclear material of one species of animal into the enucleated oocyte of a recipient animal (entire disclosure and specifically claimed in claims 1-39). Stice *et al.* teach that various combinations of species can be done and provide working examples where the oocyte is cultured for 16 hours, enucleated and donor nuclear material is transferred to the perivitelline space and fused by electrofusion (pages 35-44). The broad method claims do not require that the nuclear donor is form a differentiated cell as indicated in the declaration

therefore, this argument is found unpersuasive as it applies to the instant rejection. Moreover, since the claims are drawn to a product by process, a resulting embryo made by any means would anticipate the instantly claimed embryos.

Accordingly, Stice *et al.* anticipates the embryo encompassed by claims 12 and 14.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-14 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Prather *et al.* (Biology of Reproduction, 1987, IDS reference), Gurdon (J. Cell. Sci. , 1986), Campbell *et al.* (WO 97/07668, March 1997, IDS reference), Telford *et al.* (Molecular Reproduction and Development, 1990, IDS reference), Dominko *et al.* (Molecular Reproduction and Development, 1997, IDS reference) in further view of Stice *et al.* (WO 95/17500)

Applicants disagree with the interpretation of the teaching of Gurdon and argue that the amphibian oocyte used by Gurdon would not be predicative of the use of mammalian oocyte, in particular for the use of bovine oocyte as required in the method claims set forth in claims 1 and 13. Further, Applicants note the declaration of Dr. First indicates that the results obtained by the use of amphibian oocyte would not be predictive of nuclear transfer units made by using mammalian bovine oocyte. Further, it is noted that dependent claims require that differentiated cells be used, and this is not disclosed by Stice et al. See pages 5-6 and the declaration of Dr. First.

Examiner agrees with Applicants analysis of Gurdon that the results using amphibian oocyte would not specifically predict the outcome for the use of bovine oocyte as a recipient. However, the teaching of Gurdon is not so simple as to only indicate the effectiveness of using amphibian oocyte in transspecies nuclear transfer. Rather, Gurdon teaches that the more related the oocyte recipient/nuclear transfer unit species is phylogenetically, the better able is the resulting NT unit to be cultured. The instant claims are broad encompassing the use of any non-bovine nuclear material in generating the NT unit. The bovine oocyte, like the amphibian oocyte has certain capacities to support growth of a NT unit made by transpecies nuclear transfer. To the extent that an amphibian oocyte will only support the prolonged growth in culture of certain nuclear donors, Examiner agrees that the use of amphibian oocyte with mammalian nuclear material would not be predictive of using mammalian oocyte with nuclear material from a different mammalian species. However, the results and teachings of Gurdon clearly would lead

the artisan to predict and expect that the closer the species relationship of the donor and recipient, the more viable the resulting NT would be. Gurdon teach that transpecies nuclear transfer has been attempted for a wide variety of species of animals, and in view of the teachings of the reference as a whole provides for the use of recipient mammalian oocyte. Stice *et al.* was added in response to Applicants previous amendment. Stice *et al.* clearly teach the generation of chimeric embryos, in particular for the generation of chimeric ungulates including bovine (for example claims 3, 4) and provides evidence that at the time of filing one of skill in the art was practicing nuclear transfer and using the methodology to generate chimeric embryos (see entire disclosure and in particular claim 32-37).

Examiner agrees that Stice et al. teaches the use of undifferentiated cells as donor cells, however the broadest claims encompass the use of these cells. Moreover, combined with the teachings of the other cited references, clearly the use of differentiated cells for transpecies nuclear transfer was contemplated. As noted previously Examiner would agree that Prather does not teach transpecies nuclear transfer, however it does provide guidance and evidence for the state of the art at the time of filing for nuclear transfer into bovine oocyte was successfully done at the time of filing. The methodology for nuclear transfer and culturing of the resulting embryos as instantly claimed is taught in both Prather *et al.* and Stice *et al.* and is very analogous in all references, indicating that the conditions used by the artisan to generate and culture non-chimeric embryos would at least initially used for chimeric embryos. Each of Gurdon, Prather *et al.* and Stice *et al.* teach the nuclear transfer is possible using mammalian material, and Gurdon

and Stice *et al.* clearly teach that transpecies nuclear transfer was practiced at the time of the claimed invention was made. Gurdon teaches that optimization of conditions would be necessary to produce a chimeric embryo capable of longer term culturing or capable of progressing through embryogenesis (Gurdon-pages 310-312). Applicants arguments that one of skill in the art would not use the culture conditions normal embryos for the culturing of chimeric embryos is unpersuasive. First, the culture conditions used in the generation of chimeric embryos in both Stice *et al.* and Gurdon are the same as is used for the culturing a normal non-chimeric embryo. Further, the instant disclosure also teaches to use conditions that are well known in the art for culturing an embryo (see page 19 and compare to Stice *et al.*). A review of the art of record does not indicate that conditions for culturing chimeric embryos would be different from those for culturing a normal embryo, though Gurdon does suggest that optimization may be necessary for increase embryo development. Clearly, as indicated in the specific teachings of Gurdon and Stice *et al.* and as disclosed in the instant specification, one of skill in the art would start with the culturing conditions for a normal embryos. Additionally, improvements in the culturing conditions for a particular species of oocyte and improvements in methodology for nuclear transfer will serve as a source of optimization of the general methodology disclosed in Gurdon and Stice *et al.*

As noted in prior office actions, Campbell *et al.* provides a recent status of nuclear transfer techniques, and in particular, Campbell teaches the use of donor cells which have been arrested in Go by various methods, maturation curves of the bovine oocyte, and activation of the

NT unit by various techniques known in the art. Further, Campbell teaches that the described nuclear transfer technology can be used to generate transgenic animals as well (entire reference; summarized in abstract and specifically claimed). Additionally, Dominko *et al.* and Telford *et al.* both provide further guidance for the optimization of in using bovine oocyte. Specifically, Dominko *et al.* demonstrate that there is an increased efficiency in embryo development when the genetic material is transferred later that 8 hours of culturing (Figures 3 and 4). Examiner concedes that Telford *et al.* teach that there is a transition from maternal control (donor oocyte control) to the embryo for various species of animals and in particular, in the cow, this change occurs between 8-16 days. However, Stice et al. teaches that embryos that activation for most domestic animals will range from 16-52 hours (page 23; lines 16-27). In view of the work of Stice *et al.* and Dominko *et al.* it is clear that to establish the control of the genetic material transferred by nuclear transfer techniques, at least in the bovine, the artisan would deliver the nuclei after the 16 hour culture transition period.

Therefore, in view of the art as a whole, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to generate chimeric embryos by nuclear transfer techniques. As noted in Gurdon and Stice *et al.*, cross-species nuclear transfer has been performed for prior to the time of the claimed invention, however it was also observed that optimization of the methods wold be necessary. Campbell *et al.*, Telford *et al.* and Dominko *et al.* provide such optimization conditions detailing specific method steps and materials necessary to increase embryo development for the cow. One of skill in the art would

have been motivated to use the teachings of Campbell *et al.*, Telford *et al.* and Dominko *et al.* because at the time of the claimed invention they represented the latest and best conditions/methods available to practice nuclear transfer techniques.

Thus, the claimed invention, as a whole, was clearly *prima facie* obvious in the absence of evidence to the contrary.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (703)305-3732.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at (703)305-4051.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Dianiece Jacobs whose telephone number is (703) 308-2141.

Joseph T. Woitach

Joe Woitach
AU 1632